# Allergy Abstracts

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## Asthma and Hay Fever

**Allergy to Aspirin.** Walton, C., and Bottomley, H.: Canad. M. A. J. **64**: 187, 1951.

Aspirin sensitivity was observed in 22 of 830 successive hospital admissions (2 per cent). Since approximately 25 per cent of the admissions were children who showed no aspirin sensitivity, the adult incidence was therefore 3.5 per cent. Fifteen of these patients were women and approximately one-half of the individuals were asthmatics. Only 13 per cent of the entire group were considered to have advanced cases of asthma. Notwithstanding the accepted theory that most aspirin-sensitive patients are skin-test-negative, the authors found that from 50 to 75 per cent of their subjects showed positive reactions to direct tests with aspirin. No attempt was made to transfer these reactions. Since aspirin sensitivity can cause fatal reactions, the need for caution in the administration of all medications to asthmatic patients is stressed. R. W.

**Influence of ACTH on the Excretion of Histamine and Histidine in Patients With Allergic States or Rheumatoid Arthritis.** Rose, B., Pare, J. A. P., Pump, K., Stanford, R., and Johnson, L. G.: J. Clin. Investigation **29**: 841, 1950.

Histamine and histidine excretion in the urine were studied in 15 allergic patients (asthma, chiefly) and in 5 patients with rheumatoid arthritis before, during, and after ACTH administration. Urinary histidine increased to levels characteristic of pregnancy within 24 hours following the institution of ACTH therapy and fell to normal promptly on withdrawal of the drug. Histamine excretion in asthmatic patients, which is normally 0.5 to 0.7 mg. in 24 hours,

increased to from 4 to 7 mg. and returned to normal as the asthmatic symptoms subsided. In 4 rheumatoid arthritic patients there was little change in histamine excretion; in the fifth arthritic a moderate rise was observed. K.

**Surveys of Ragweed Pollination in the New York Metropolitan District in 1948 and 1949.** Wiseman, R. D., Siegel, B. B., Glazer, I., Chait, R. A., and Walzer, M.: New York State J. Med. **50**: 2552, 1950.

In 1948, pollen surveys were conducted at 17 stations in the New York metropolitan area. In 1949, 16 stations were surveyed. The totals of the averages of the daily ragweed pollen counts for the 8 stations in New York City proper were approximately the same for both years. However, the timing of maximum pollination was different each year. In 1948, several distinct peaks were noted in late August, whereas in 1949 the only significant ragweed pollen spill occurred on September 1. In the order of diminishing pollen concentration, the 5 boroughs of New York City were rated as follows: Queens, Staten Island, Manhattan, Brooklyn, and the Bronx. The area of New Jersey, west and southwest of New York City, showed the greatest pollen density within the metropolitan area. This fact undoubtedly accounted for high counts in New York City on those days when high winds were blowing from the west and southwest during the period of pollination. Seasonal totals in Brooklyn for 1948 and 1949, as measured by the old shelter technique, were about 70 per cent of a 14-year average. Meteorologic conditions during the prepollination and pollination periods of these 2 years probably accounted for these low pollen counts. AUTHOR'S SUMMARY.

**Periarteritis Nodosa. Report of a Case.** Leffler, R. J.: U. S. Armed Forces M. J. **1**: 1503, 1950.

A 47-year-old white woman was hospitalized with a complaint of asthma of 30 months' duration, anorexia, and extreme weakness. She had a past history of hypersensitivity to penicillin and other drugs. Blood studies revealed a macrocytic hypochromic anemia and an eosinophilia of 24 per cent. The sedimentation rate was elevated. Urinalysis showed albuminuria, fixed low specific gravity, and showers of red cells. Radiologic examinations showed pulmonary emphysema and fibrosis. Although there was temporary slight improvement on supportive therapy, the asthma then became more severe; she developed transient numbness and hyperesthesia, a right flaccid hemiplegia, and died 8 months after admission. Post-mortem examination revealed the following: a ruptured aneurysm of the left superior cerebellar artery, with a large clot in the area; hemorrhage and destruction in the region of the left internal capsule and basal ganglia of the brain; microscopic evidence of periarteritis nodosa in the vessels of the liver, colon, adrenals, brain, ovaries, and heart. The kidney showed changes attributable to chronic glomerulonephritis. The lungs showed arteriosclerosis of the pulmonary arteries and fibrosis of the lung parenchyma with the formation of thick masses of granulation tissue and many foreign body giant cells suggestive of reaction to lipoid material. Apparently, there was an association of several disease processes in this case suggestive of a common etiological basis. E. W.

**Sudden Death From Asthma.** Walton, C., Penner, D., and Wilt, J.: Canad. M. A. J. **64**: 95, 1951.

Thirteen individuals who had died suddenly from asthma were autopsied. In 9 of these patients, heavy sedation with morphine, Demerol, or intravenous

anesthetics preceded the fatal termination. The pathologic findings were the same in the intrinsic and extrinsic types of asthma. Age did not modify the findings except that the older individuals showed more emphysema. Five features were found consistently in all cases: voluminous lungs, mucus plugging, prominent hyalinized basement membranes, emphysema, and eosinophilic infiltration of the bronchial walls. R. W.

**On Universal Reactions in Connection With Treatment of Asthmatic Children With Bacterial Vaccines.** Fleusborg, E. W.: Acta paediat. **39**: 192, 1950.

The literature on the incidence of constitutional reactions during treatment with bacterial vaccines was reviewed. One or more reactions occurred in 42 (26 per cent) of 162 children treated. The highest number of reactions occurred in children under 6 years of age, especially during the first 3 years of life. The symptoms of the constitutional reactions observed consisted of asthma and hyperpyrexia. Twenty-four (15 per cent) had a constitutional reaction after the first dose of vaccine. Vaccine reactions were usually of the delayed type. The average time of onset of the reaction was 48 hours after the injection; the earliest reaction occurred within 6 hours.

The author stated that the initial dose of vaccine administered to children should be very small. The initial dose should not be more than 5,000 bacteria in children up to the age of 4 years. A 1-year-old child died from a constitutional reaction following the injection of a dose of 2,600 bacteria, although this same dose had previously been well tolerated. H.

## Dermatology

**A Coccidioidin Patch Test.** Cohen, R., and Gifford, M. A.: J. Pediat. **35**: 601, 1949.

Attempts were made to develop a patch test for coccidioidomycosis. Coccidioidin antigen was prepared according to Vollmer's technique for preparing the tuberculin patch test materials. Of 120 subjects known to be positive reactors to the intracutaneous test, 22 per cent showed positive reactions to the patch tests. When the antigen was incorporated in an ointment and applied as a patch test to 100 known positive reactors, only 4 per cent reacted positively. The unreliability of the coccidioidin patch test could not be explained. J. S.

**Atopic Dermatitis. II. Role of the Sweating Mechanism.** Tuft, L., Tuft, H. S., and Heck, V. M.: J. Invest. Dermat. **15**: 333, 1950.

In 2 patients with atopic dermatitis, the writers studied the effect of the inhalation of specific excitants upon the sweating mechanism. When these subjects were dusted with an iodine-starch powder, it was observed that the areas commonly involved in atopic dermatitis were those which showed the most pronounced sweating as indicated by the starch-iodine reaction. This reaction could be inhibited by the intramuscular injection of 30 mg. of Benadryl one hour prior to exposure to the specific allergen. A biopsy performed in one case confirmed the diagnosis of atopic dermatitis and showed occasional horny plugging of some of the sweat ducts, indicating involvement of these glands. It was concluded that the production of dermatitis by the inhalation of specific allergens may be associated in some way with disturbances in the sweating mechanism. R. W.

**Studies in Eczematous Sensitizations. III. The Development in Species Other Than Man or the Guinea Pig.** Rostenberg, A., Jr., and Haeberlin, J. B., Jr.: J. Invest. Dermat. **15**: 233, 1950.

Attempts were made to induce eczematous sensitization in dogs, ferrets, hamsters, and rabbits by the repeated application of dilute solutions of 2:4 dinitrochlorobenzene and paranitrosodimethylaniline to the skin. Equivocally positive results were obtained in dogs and ferrets, but hamsters and rabbits showed essentially negative reactions. The difficulties in interpreting such reactions and in differentiating between true sensitization and primary irritation are discussed. R. W.

**Allergic Eczematous Contact-Type Dermatitis Caused by Rubber Sponges Used for the Application of Cosmetics.** Furman, D., Fisher, A. A., and Leider, M.: J. Invest. Dermat. **15**: 223, 1950.

Twenty-six cases of eczematous dermatitis primarily involving the skin of the face were observed in women between the ages of 15 and 30 years. The rash was most prominent in the areas about the mouth and eyes, where the greatest concentration of cosmetics was applied. Many of the patients were thought to have seborrheic dermatitis or neurodermatitis. In those cases where a diagnosis of contact dermatitis was made, cosmetics were thought to be the etiologic factor. However, when patch tests were made on these patients, positive reactions were obtained in all cases with the rubber sponges used for the application of cosmetics. As soon as the use of these sponges was discontinued, the dermatitis quickly cleared. In most instances, patch tests performed with cosmetics gave negative results. R. W.

**Antihistamines in Allergic and Non-Allergic Dermatoses.** Davis, J.: Bull. New York Acad. Med. **26**: 686, 1950.

Six hundred and sixty-six patients were treated with various antihistaminics in order to evaluate their relative effectiveness in relieving allergic and nonallergic dermatoses. The drugs were used both orally and locally. The results indicated that antihistaminics administered orally were most effective in the control of urticaria, while topical applications were most effective in such conditions as atopic dermatitis or pruritus vulvae, ani, and scroti. Local therapy with antihistaminics is contraindicated in acute dermatoses, especially in contact dermatitis such as poison ivy. Side reactions from oral administration occurred in approximately 20 per cent of the cases. The incidence of untoward reactions following local applications was 5 per cent. R. W.

**Cutaneous Sensitivity to Monoglycerol Para-Aminobenzoate.** Curtis, G. H., and Crawford, P. F.: Cleveland Clin. Quart. **18**: 35, 1951.

Following the application of a sunburn lotion, a 40-year-old woman developed lichen ruber planus. Three months later when the skin was clear, 100 mg. of para-aminobenzoic acid was taken orally. The next day she developed erythema, pruritus, and swelling of the dorsa of the hands. Subsequent handling of the sunburn preventative produced a severe contact type of eruption. Monoglycerol para-aminobenzoate was shown by patch tests to be the sensitizing ingredient in the lotion. Cross sensitivity was demonstrated to para-aminobenzoic acid, certain of its alkyl derivatives, and such structurally related dyes as aniline and paraphenylenediamine. The immunochemical theory of complementariness for the precipitin reaction, as suggested by Pauling and associates, may account for cross sensitization by the interaction of the cellular proteins

(antibodies) and the hapten-protein groups formed from sensitizing compounds in the epidermis. The haptenic groups assume molecular spatial relationships providing certain corresponding areas for reaction with the stable configuration of the complementary antibody polypeptid chains. Thus, for every antigen a specific complementary antibody is present. The authors include a compilation of chemicals arranged in groups and in the order of their frequency in producing positive reactions. From this table, structurally related chemicals may be selected for a rapid survey by the patch test technique to determine the trend of cross sensitizations. F.

**Photosensitization Induced by Monoglycerol Para-aminobenzoate.** Satulsky, E. M.: Arch. Dermat. & Syph. **62**: 711, 1950.

A diffuse generalized exfoliative erythrosquamous dermatitis appeared in a 21-year-old man, 24 hours after the application of a commercial sun tan lotion to the skin and exposure to sunshine. When the lesions had cleared, a patch test with the sun tan lotion was made on the patient's back. The same lotion was applied to the flexor surfaces of the forearms and these parts were then exposed to sunlight. At 48 and 72 hours after application, the patch tests on the back showed negative reactions. Large edematous, erythematous areas with large bullae and vesicles developed on the forearms.

A month later, exposure of the forearms to ultraviolet radiation following local application of the same sun tan lotion resulted in the same type of lesion after 48 hours.

Patch tests performed on the back with each of the 8 ingredients of the sun tan lotion gave negative reactions. The individual ingredients, when applied on the forearm and exposed to ultraviolet radiation at 30 inches for 90 seconds, failed to produce any reactions, except for the monoglycerol ester of para-aminobenzoic acid. The latter caused a marked reaction. C.

**A Reaction to Local Anesthesia in a Patient Sensitized to P-Phenyldiamine.** Sidi, S., and Dobkevitch, S.: Bull. Soc. franç. de dermat. et syph. **3**: 269, 1949.

A female hairdresser with a previous history of sensitization to p-phenyldiamine reacted with a violent acute eczematous reaction and high fever following an injection of procaine for a dental extraction. It is suggested that cross sensitization should be considered as a possibility among the following group of substances; paraphenyldiamine, sulfonamide 1162 F., synthetic anesthetics of the procaine group, para-aminobenzoic acid, para-aminosalicylic acid, and the sulfones. H.

**Dermatitis From Orange I in a Candy Factory.** Goldsmith, N. R.: Arch. Dermat. & Syph. **62**: 695, 1950.

An outbreak of dermatitis in a group of people working in a candy factory was traced to tinted sugars used in the preparation of Halloween candies. Negative reactions were obtained to patch tests performed with the individual components of the candies, with one exception. Tests performed with Orange I (the sodium salt of p-sulfobenzene azo-alpha-naphthol) gave positive reactions. C.

**Cutaneous Hypersensitivity to Tear Gas (Chloroacetophenone).** Madden, J. F.: Arch. Dermat. & Syph. **63**: 133, 1951.

A contact type of dermatitis involving the legs was traced to the use of tear gas bombs for eradication of rodents. A purposeful exposure of the legs to tear gas was followed, within 8 hours, by the appearance of typical contact dermatitis on the exposed areas. C.

## Otorhinology and Ophthalmology

**Organ-Specific Antigens in Embryonic Rudiment of the Eye Lens.** Ten Gate, G.: Nederl. tijdschr. v. geneesk. **29**: 2136, 1950.

By means of precipitin tests, antigens of adult lens were demonstrated in isolated embryonic lenses. Lens antigens from 60- to 74-hour chick embryos and stage 21 embryos of frogs yield positive precipitin reactions with rabbit antisera prepared by immunization with lens material from adult fowls and frogs. The author concluded that adult lens protein is present as soon as lens vesicle is formed, even before separation from the epidermis occurs. H.

## Miscellaneous Allergies

**Reactions to Para-Aminosalicylic Acid.** Kierland, R. R., and Carr, D. T.: Proc. Staff Meet., Mayo Clin. **24**: 539, 1949.

Four cases are recorded in which untoward reactions developed after the administration of para-aminosalicylic acid for periods varying from 8 days to 6½ weeks. Three of these patients exhibited a diffuse scarlatiniform eruption and one developed a fixed type drug eruption involving the penis. Fever accompanied the reactions in 2 cases. Intracutaneous and patch tests made with para-aminosalicylic acid gave negative reactions. One patient was given para-aminobenzoic acid orally with no untoward reaction. However, when sodium salicylate was administered to this patient, pruritus and a scarlatiniform rash developed. The authors considered this patient sensitive to the salicylic acid radical of the para-aminosalicylic acid. B. S.

**Local Cellular Responses in Experimental Hypersensitivity.** Angevine, D. M., and Seastone, C. V.: Am. J. Path. **26**: 1011, 1950.

Some investigators have reported a monocytic cellular response in the tissues of sensitized animals and in bacterial allergy of the delayed or tuberculin type. Others have found no particular cellular response characteristic of bacterial allergy of the delayed type.

In the present report, guinea pigs sensitized with egg albumin and rabbits sensitized with B.C.G. were studied. The skin and peritoneum were examined in all animals. Monocytes were found in variable numbers, but they were not exclusively present or even predominant. Rabbits sensitized with B.C.G. and later tested by the injection of OT or PPD into the skin and peritoneal cavity developed an inflammatory response dominated by the neutrophilic granulocyte. J. S.

**Skin Tests During Para-Aminosalicylic Acid Treatment of Pulmonary Tuberculosis.** Zanussi, C., Salotto, B., and Busani, L.: Riforma med. **63**: 1181, 1949.

Tuberculin tests were performed on 27 patients before, during, and from 14 to 90 days after treatment with para-aminosalicylic acid. In all cases with a favorable prognosis following treatment, the tuberculin reaction was stronger at the end of the treatment course. The authors attributed this phenomenon to the development of increased resistance by the patient and to the probable widespread destruction of bacilli by para-aminosalicylic acid, resulting in saturation of the body with breakdown products of the tubercle bacilli. H.

**Action of Adrenocorticotropic Hormone (ACTH) in Experimental Allergic Encephalomyelitis of the Guinea Pig.** Moyer, A. W., Jervis, G. A., Black, J., Koprowski, H., and Cox, H. R.: Proc. Soc. Exper. Biol. & Med. **75**: 387, 1950.

Guinea pigs were injected with rabbit brain emulsion plus adjuvants and then treated with ACTH for varying periods of time. When the hormone was given for the first time 13 days after the injection of antigen, all of the animals were protected against allergic encephalomyelitis. As the number of injections of ACTH diminished, an increase was noted in the number of animals affected and the extent of the neurologic lesions. Two doses of ACTH given on the first 2 days after the injection of antigen afforded more protection than an equal dose given on the tenth and eleventh days. It is suggested that the hormone inhibits allergic encephalomyelitis by modifying vascular reactivity. B. S.

**The Tuberculin Reaction in Different Parts of the Skin and Tuberculin Sensitivity in Rheumatoid Arthritis.** Wasz-Hoeckert, O.: Acta paediat. **39**: 93, 1950.

Experimental studies were conducted to determine the relationship between tuberculin sensitivity and various physiologic conditions. The author found that the technical error in the Mantoux test was 15 per cent. The tuberculin reaction in adults was definitely stronger on the back than on the forearm. The difference in reactions on the dorsal and volar sides of the forearm was only 10 per cent. In children, no consistent pattern could be established. Anatomic differences of skin areas did not play a part in the results obtained with repeated Mantoux tests. H.

**Allergic Encephalitis and Its Possible Relationship to Human Disease.** Peers, J. H.: Am. J. Clin. Path. **20**: 503, 1950.

A brief review of allergic encephalitis is presented. The parenteral injection of heterologous brain tissue, particularly with adjuvants, induces an encephalitis characterized by ascending paralysis in monkeys, rabbits, and guinea pigs. On section of the brain, venous dilatation and perivascular infiltration with partial demyelination of included white matter are noted. The disease resembles human postvaccinial encephalitis. K.

**Cottonseed Protein vs. Cottonseed Oil Sensitivity. II. A Case of Cottonseed Oil Sensitivity.** Randolph T. G., and Fisk, W. N.: Ann. Allergy **8**: 5, 1950.

Sensitivity to cottonseed oil in the absence of sensitivity to cottonseed protein was observed in 2 patients. In the first patient, a 38-year-old physician, the experimental ingestion of cottonseed oil evoked headache, abdominal discomfort, fatigue, and a drop in the total leucocyte count. This patient also had nasal symptoms and showed positive skin reactions to dust, feathers, and orris root. In the second patient, a 59-year-old housewife, experimental feeding of cottonseed oil produced drowsiness, headache, myalgia, abdominal cramps, diarrhea, and a leucopenia. Skin tests with cottonseed extract gave negative reactions in both patients. The elimination of cottonseed oil from the patients' diets produced considerable improvement in the symptomatology of both individuals. E. W.

## Anaphylaxis

**The Effect of Antihistaminics on Mice Hypersensitive to H. Pertussis Vaccine.** Parfentjev, I. A.: Yale J. Biol. & Med. **23**: 28, 1950.

Mice treated with *Hemophilus pertussis* vaccine became highly sensitive to both histamine and *H. pertussis* protein-antigen. White mice weighing from 22 to 26 grams were sensitized by the intra-abdominal injection of *H. pertussis* vaccine. Challenging doses of histamine were administered intravenously after sensitization and challenging doses of a detoxified formalin filtrate of a culture of *H. pertussis* were administered 11 or 12 days after initial sensitization. Thephorin was either injected intra-abdominally 15 minutes prior to the challenging dose or administered by stomach tube in 2 doses about 4 hours prior to the administration of the challenging substance. Thephorin, administered intra-abdominally in doses of 25 mg. per kilogram, protected mice against 12 lethal doses of histamine. When Thephorin was administered by mouth in doses of 2 × 50 mg. per kilogram and 2 × 100 mg. per kilogram, it protected sensitized animals for a period of more than 4 hours against doses of histamine at least 3.5 and 6.2 times the 50 per cent lethal dose. Thephorin in doses of 2 × 100 mg. per kilogram also inhibited the anaphylactic shock produced by *H. pertussis antigen*. More than 50 per cent of the animals pretreated with Thephorin survived, as compared to a 10 per cent survival in the control animals. It is suggested that mice sensitized with vaccine seem particularly suitable for studies of bacterial allergy, since they can be tested both for histamine sensitivity and the anaphylactic state. E. W.

**Histamine Antagonists. XV. Comparative Experimental Studies of Certain Antihistaminic Compounds.** Feinberg, S. M., Malkiel, S., Bernstein, T. B., and Hargis, B. J.: J. Pharmacol. & Exper. Therap. **99**: 195, 1950.

Twenty-five antihistamine drugs were subjected to 4 selected tests in guinea pigs under uniform conditions. These tests included the intraperitoneal injection of various doses of the drugs followed by (1) a challenging intravenous injection of histamine, or (2) the intravenous injection of horse serum in serum-sensitive animals, or (3) exposure to histamine aerosol. In addition, all drugs were administered in aerosol form to animals which were then exposed to histamine aerosol. The administration by aerosol of some antihistamines, such as Phenergan, Tagathen, Bromothen, and Pyrrolazate, was found to be too irritating to be tolerated in doses adequate for protection. A much larger dose was required for protection against anaphylaxis than against histamine, possibly because the amount of histamine released in anaphylaxis is much more than 100 minimum lethal doses of histamine or possibly because histamine is not the primary cause of anaphylactic death. Orthoxine, which has no specific antihistaminic action, was found to give some protection against histamine shock but none against anaphylaxis. There was a rough but not exact correlation between clinical potency and the efficacy of the drugs as judged by the tests. Pyribenzamine, Chlor-Trimeton, Neoantergan, Chlor-neoantergan, Thenylene (Histadyl), Tagathen, and p-fluorobenzyl-DPE were all effective with each of the techniques tested. In contrast, Antistine and Neohetramine showed a low degree of protection against histamine shock, histamine aerosol, and anaphylaxis. These studies failed to take into account toxicity factors, which are of importance clinically. K.

**The Mechanism of the Anaphylactoid Phenomenon.** Gross, P., and Brown, J. H. U.: Am. J. M. Sc. **221**: 46, 1951.

The shock reaction which may occur as the result of intravenous injections of foreign material closely resembles anaphylactic shock and is termed

the anaphylactoid phenomenon. This reaction is characterized by pulmonary vascular occlusion (involving the smallest vessels) and a resultant dilatation of the right side of the heart. In rabbits, the intravenous injection of small doses of finely divided chemically inert materials produces rapid death suggestive of embolism. Such fatalities were shown to be the result of pulmonary vascular occlusion by bulky aggregates formed by the absorption of plasma proteins onto the finely divided particles. Chemical analysis of these aggregates demonstrated the presence of adsorbed protein. An inverse relationship was shown to exist between the particle size and the amount of protein adsorbed. Pulmonary vascular occlusions identical with those seen in animals dying of typical anaphylactoid phenomenon could be produced in rabbit lungs perfused with plasma, free of fibrin and formed elements, but containing small amounts of finely divided particulate matter. F.

**Effects of Cortisone, Hyaluronidase, Desoxycorticosterone, and Artisone on Experimental Serum Disease in Rabbits.** Seifter, J., Ehrich, W. E., Begany, A. J., and Warren, G. H.: Proc. Soc. Exper. Biol. & Med. **75**: 337, 1950.

Cortisone administered to horse-serum-treated rabbits depressed the Arthus reaction and prevented arteritis and carditis in the majority of animals. Glomerular nephritis was not prevented in these animals. The cortisone effect appeared to be mediated primarily by a depression of antibody formation through destruction of antibody-forming cells and also by an antipermeability effect on ground substance. Hyaluronidase given to horse-serum-treated animals depressed the Arthus reaction, diminished glomerular nephritis, but enhanced arteritis and carditis. These observations were explained by the capacity of hyaluronidase to weaken ground substance barriers and thus divert antigen and antibody from the kidneys to the general vascular bed. Desoxycorticosterone (DCA) and Artisone had no effect on the histologic manifestations of serum disease. However, DCA caused a depression of the Arthus reaction, possibly through its hyaluronidase-like effect upon the ground substance. B. S.

## Pharmacology, Physiology, and Pathology

**A Neurologic Evaluation of the Cutaneous Histamine Reaction.** Cooper, I. S.: J. Clin. Investigation **29**: 465, 1950.

The cutaneous reaction to histamine in normal and anesthetic areas was studied in 50 young men with a variety of neurologic lesions. Partial transection of a peripheral nerve did not affect the response, whereas, following complete transection, there was an initial red reaction and wheal but no spreading flare. In 3 cases of severe poliomyelitis the histamine reaction was normal, indicating that the anterior horn cells and "final common pathway" do not play a significant role in producing the spreading flare. In 9 of 10 cases of complete spinal cord transection, the spreading flare was absent below the level of transection. The tenth patient developed a wheal on the forearm measuring 27.5 by 8 cm. and a wheal on the thigh, below the transection, of 6 by 6 cm. within 5 minutes. He also experienced flushing and headache. Incomplete transection of the spinal cord failed to influence the cutaneous histamine response even when superficial sensation was absent. Sympathectomy with impairment of sweating did not affect the histamine reaction. Syringomyelia with destruction of the anterior commissure of the cord and loss of ability to perceive pain or temperature did not interfere with the triple histamine re-

sponse. In 2 cases of cerebral damage (hydrocephalus, deep concussive coma followed by decerebrate rigidity), the histamine reaction showed a large initial flare which did not increase after 30 seconds. It is suggested that one or more centers cephalad to the pons affect the spreading flare phase of the triple reaction. Histamine reaction proceeded normally in skin which was anesthetic because of hysteria.

It was concluded that the axone reflex theory does not adequately explain the spreading flare phase of histamine reaction and that an isolated spinal reflex arc is unable to mediate the secondary flare. It is postulated that the reaction is carried by a suprasegmental reflex arc, reaching to the diencephalon or above, with the afferent and efferent impulses carried in the dorsal nerve roots. K.

**The Pharmacologic Action of Some Analogs of 1-(3, 4-Dihydroxyphenyl)-2-Amino-1-Butanol (Ethylnorepinephrine).** Lands, A. M., Ludnena, F. P., Grant, J. I., and Ananenko, E.: J. Pharmacol. & Exper. Therap. **99**: 45, 1950.

Ethylnorepinephrine (Butanefrine) is an effective bronchodilating drug which exhibits less cardiovascular activity than Isuprel. Butanefrine and 3 of its analogs known as WIN 3046, WIN 515, and WIN 713, were found to lower blood pressure and to increase the heart rate of barbitalized dogs to a lesser degree than Isuprel by a ratio of from 1:40 to 1:80. Two of the analogs were more effective bronchodilators than Butanefrine and about one-half as potent as Isuprel when tested on the histamine-constricted guinea pig lung. It was interesting to note that Butanefrine was only one-sixth as effective as epinephrine in counteracting histamine constriction in the perfused guinea pig lung and one-sixtieth as effective as Isuprel. In counteracting bronchospasm in the histamine-aerosolized guinea pig, Isuprel was about 75 to 100 times more active than Butanefrine and epinephrine was 50 times more active. The Butanefrine derivatives very weakly counteracted spontaneous motility of the ileum of dogs and of guinea pigs. Two derivatives counteracted pituitrin contracture of guinea pig and dog uteri to a greater extent than Butanefrine and exhibited an activity approximately the same as that of epinephrine and Isuprel in this test. Spontaneous muscular activity of rats was not increased by butanefrine or its derivatives. Their acute intravenous toxicity in mice was comparable to that of Isuprel and less than that of epinephrine. It is suggested that "The structural requirements for myocardial stimulation differ from those favorable for sympathetic excitatory or inhibitory action." K.

**Experimental Hypersensitivity in the Rabbit. Effect of Inhibition of Antibody Formation by X-Radiation and Nitrogen Mustards on the Histologic and Serologic Sequences and on the Behavior of Serum Complement, Following Single Large Injections of Foreign Proteins.** Schwab, L., Moll, F. C., Hall, T., Brean, H., Kirk, M., Hawn, C. V. Z., and Janeway, C. A.: J. Exper. Med. **91**: 505, 1950.

Rabbits heavily irradiated with roentgen rays both prior to and shortly after a single sensitizing injection of either bovine serum gamma globulin or bovine serum failed to produce any discernible circulating precipitin antibody. Circulating antigen was still present after a 2-week interval. All the control animals developed antibodies within 2 weeks and none showed circulating antigen at this time. In another study, 5 rabbits received nitrogen mustards prior to and following a sensitizing dose of gamma globulin. Four of these animals failed to develop antibodies by the fourteenth day and at this

time still showed antigen in the blood. Controls showed antibody present and no circulating antigen during the same period.

Serum complement levels were determined every 2 or 3 days throughout the sensitization period in gamma globulin-sensitized animals and in normal animals. Then the animals of both test and control groups were sensitized with a single injection of bovine serum albumin and complement titrations were again made. In all 4 gamma globulin-sensitized animals, the complement level fell sharply between the seventh and ninth days. This was the time at which antigen was disappearing from the circulation and antibody was appending in the circulation. The complement titer then increased to normal levels. In another experiment, comparison was made of complement levels, antigen, antibody levels, and tissue changes in animals injected with gamma globulin, with and without various doses of nitrogen mustards, and in animals injected with nitrogen mustard alone. Nitrogen mustards in sufficient dose to suppress antibody formation also suppressed the characteristic decline of complement activity and the development of tissue lesions. In a similar experiment using x-radiation to prevent antibody formation, the fall in complement was inhibited and the development of renal lesions was prevented in all 8 animals so studied.

It was concluded that the fall in complement titer observed in this study was due to fixation of complement in vivo by a reaction between antigen and antibody. The data obtained favor the concept that characteristic tissue lesions are due to a reaction between circulating antibody and antigen, fixed in or on the cells. The possible significance of serum complement in the pathogenesis of foreign serum tissue lesions is discussed. K.

**Effect of Antihistamine Drugs on the Adrenal Cortical Response to Histamine and to Stress.** Tepperman, J., Rakieten, N., Birnie, J. H., and Diermeier, H. F.: J. Pharmacol. & Exper. Therap. **101**: 144, 1951.

When Benadryl, Pyribenzamine, or Phenoxadrine is administered orally to rats in doses of 30, 30, and 50 mg. per kilogram body weight, respectively, there is no significant change in adrenal ascorbic acid concentration. Intraperitoneal injection of histamine lowers adrenal ascorbic acid concentration. The degree of fall in ascorbic acid concentration is diminished when the animals are pretreated with Pyribenzamine or Phenoxadrine, but is not modified by pretreatment with Benadryl. Benadryl administration consistently produced a slight hyperglycemia, whereas Phenoxadrine and Pyribenzamine did not. Carbon tetrachloride administered intraperitoneally lowers adrenal ascorbic acid concentration, but this stress response was not modified by any one of the 3 antihistamines tested. A complicating factor encountered in these experiments was the wide variability of response to histamine in individual rats. Typically, the rat undergoes hypotension following histamine injection, the degree being roughly characteristic of the individual rat. However, one rat was found to have a 20 mm. rise in blood pressure after the intraperitoneal injection of histamine (100 mg. per kilogram of body weight). It was concluded that the antihistamines cannot be regarded as an entity with respect to their action on the histamine-stimulated adrenal gland. K.

**Comparison of the Anterior Pituitary-Adrenal Cortical Stimulating Effect of U. S. P. Epinephrine, Synthetic L-Epinephrine, and Nor-Epinephrine.** Madison, L. L.: J. Clin. Investigation **29**: 789, 1950.

The adrenal medulla secretes both epinephrine and nor-epinephrine, the latter being present to the extent of from 10 to 35 per cent in commercial

U. S. P. epinephrine. Eosinophil blood levels were studied in fasting human subjects before and 4 hours after the subcutaneous injection of 0.3 ml. of 1:1000 U. S. P. epinephrine, nor-epinephrine, synthetic l-epinephrine, or a saline control. The average per cent decline in eosinophil levels was 54.9 after U. S. P. epinephrine (32 to 70 per cent range), 47.2 after l-epinephrine (33 to 70 per cent range), 8.2 following nor-epinephrine (plus 31 to minus 29 per cent) and 8.35 following the saline injection (plus 12 to minus 29 per cent). The authors concluded that the eosinopenic effect of U. S. P. epinephrine depends on its l-epinephrine content which is the anterior pituitary-adrenal cortical stimulant, whereas nor-epinephrine does not possess this property. K.

**The Mechanism of Apnea Following Intravenous Injection of Various Antihistaminic Compounds; Its Relation to Their Chemical Structure.** Aviado, D. M., Jr., Pontius, R. B., and Li, T. H.: J. Pharmacol. & Exper. Therap. **99**: 425, 1950.

Benadryl administered intravenously to dogs caused an immediate inhibition of respiration lasting about 5 seconds which was followed by rapid, shallow breathing. Vagotomy abolished the apneic reaction. In an effort to locate the site of this reaction, dogs were anesthetized and subjected to cardiac catheterization. Small doses of Benadryl injected into the pulmonary artery elicited the apneic response. There was no response when the drug was injected into the left ventricle. Reversible cold block of the ipsilateral vagus prevented the reaction. It was concluded that there are chemoreceptors located in the lungs which are responsible for the apneic reaction. Such drugs as Pyribenzamine, Diatrin, Hetramine, Chlorothen, and pyranisamine also produce the apneic response. Benadryl administered by inhalation does not produce apnea. Veratridine, on the other hand, affects these chemoreceptors both from vascular and alveolar sides. Its action decreases with repeated administration. Such tachyphylaxis does not occur with the antihistamines. The antihistamines still can cause apnea after resistance to veratridine has developed, indicating that the chemoreceptors have not been paralyzed by this drug. It was noted that foreign serum also affects chemoreceptors in the lungs. K.

**So-called "Lupus Erythematosus Inclusion Phenomenon" of Bone Marrow and Blood. Morphologic and Serologic Studies.** Berman, L., Axelrod, A. R., Goodman, H. L., and McClanghry, R. I.: Am. J. Clin. Path. **20**: 403, 1950.

The authors verify earlier reports that "The LE cell, seen in the marrow smears of patients with acute disseminated lupus erythematosus, was practically always a mature polymorphonuclear neutrophile which appeared to have phagocytized a homogeneous purple-staining mass of chromatin material (Wright's stain) . . ." Similar homogeneous masses are present in the marrow and 2 or more neutrophils are likely to be clustered about them. Present observations indicate that such masses may also be found in band cells, eosinophils, monocytes, and lymphocytes. Lupus erythematosus (LE) cells occur occasionally in patients without lupus erythematosus but, in such instances, there are fewer than 10 LE cells per 500 band cells plus polymorphonuclear neutrophils. The LE cells and cloudy masses are more readily found in marrow specimens treated with anticoagulant and centrifuged. The writers also confirmed the fact that plasma from patients with acute disseminated lupus erythematosus, when added to normal marrow cells, is capable of provoking the appearance of typical LE cells. This effect is augmented on re-use

of the plasma, possibly because of the accumulation of proteolytic substance from the breakdown of marrow cells. Human serum containing the LE factor also induces the formation of LE cells when mixed with marrow from animals (opposum, guinea pig, and rabbit). The LE serum factor was found in the gamma globulin fraction of serum and was detected 4 hours post-mortem in one case.

Splenectomy in one patient failed to alter either the occurrence of LE phenomena in marrow smears or the LE serum activity. K.

**The Effect of Sensitization and X-Radiation on the Metabolism of $I^{131}$ Labeled Proteins.** Dixon, F., Bukantz, S., and Dammin, G.: Science **113**: 274, 1950.

Rabbits were injected intravenously with various combinations of radioiodinated proteins and the antigen excretion levels from the blood stream were determined by measuring the amount of radioactivity remaining in the blood and the various tissues. The results showed that nonimmunized animals take about 9 days to clear the blood stream of radioactivity, whereas immunized animals show a rapid decline in blood protein levels after the fourth day. Rabbits radiated prior to immunization required about the same time to excrete the antigen as normal controls. After comparing the results obtained with different techniques of employing $I^{131}$ and measuring the amount of iodide excreted in the urine, the authors concluded that $I^{131}$ labeled proteins are a very reliable tool for immunologic investigative procedures. R. W.

**Effects of Cortisone and ACTH Therapy on Eosinophils of the Bone Marrow and Blood.** Rosenthal, R. L., Wald, N., Yager, A., and Litwins, J.: Proc. Soc. Exper. Biol. & Med. **75**: 740, 1950.

Eosinophil counts were made on bone marrow and peripheral blood obtained from 7 patients with nonhematologic diseases before and during therapy with cortisone or ACTH. All subjects showed a decrease in the peripheral blood eosinophils varying from 64 to 100 per cent during hormone therapy. The bone marrow eosinophil counts showed consistent increases ranging from 42 to 372 per cent. The differential counts of the marrow, however, showed no change in the percentage of eosinophilic cells in relation to the nucleated cells. Cortisone and ACTH probably increase the rate of removal of eosinophils from the blood without affecting their production by the bone marrow. B. S.

**Pulmonary Infiltration and Blood Eosinophilia in Children (Loeffler's Syndrome). A Review With Report of Eight Cases.** Nemir, R. L., Heyman, A., Gorvoy, J. D., and Ervin, E. N.: J. Pediat. **37**: 819, 1950.

Eight cases of Loeffler's syndrome are presented. These cases illustrate the varied clinical picture of the disease, despite the fact that pulmonary infiltration and eosinophilia occurred in all. Five of the cases were mild and corresponded to Loeffler's original description. In the other 3, the disease was chronic and persisted for months. Three cases were at first mistakenly diagnosed as miliary tuberculosis. Intestinal parasitism was found in 7 of the patients. The authors concluded that Loeffler's syndrome is an allergic manifestation in which the major shock organ is the lung. The multiple etiologic agents described can be divided into extrinsic and intrinsic factors. Among the latter, bacterial infection and helminthiasis seem to play a prominent role. J. S.

## Miscellaneous

**ACTH and Cortisone in Diffuse Collagen Disease and Chronic Dermatoses. Differential Therapeutic Effects.** Irons, E. N., Ayer, J. P., Brown, R. G., and Armstrong, S. H., Jr.: J. A. M. A. **145**: 861, 1951.

Sixteen patients suffering from various diffuse "collagen diseases" were treated with ACTH and cortisone. Both medications were compared with respect to their therapeutic effect and studies were made to determine the relationship of therapeutic effects to complications in terms of dosage and metabolic variables. Bacteriologic studies showed the frequent occurrence of pathogenic organisms in patients with diffuse lupus erythematosus. In these cases, antibiotic therapy was often successful and obviated the necessity for the use of ACTH and cortisone. Immunologic studies failed to show significantly high agglutinin titers for bacterial antigens prepared from organisms isolated from the patients under observation. ACTH therapy failed to influence these titers. No significant changes were observed in the complement levels of successfully treated patients. The latter suggests that ACTH and cortisone do not act by changing the availability of complement for the antigen-antibody reactions which may be involved in these diseases. Ascorbic acid-loading tests showed that the rate of ascorbic acid utilization was apparently increased during the administration of both medications.

A comparison of the clinical responses to the drugs showed that ACTH produced the most favorable results. In diffuse lupus erythematosus, because of the high incidence of complications with long-term ACTH therapy, remissions were best sustained with cortisone. In the treatment of certain of the chronic dermatoses, cortisone was ineffective, but the high dosages of ACTH necessary to achieve good results were productive of untoward side effects when used over long periods.

The eosinophil response to ACTH and cortisone did not appear to be a reliable indicator for predicting clinical responsiveness. Excellent therapeutic results were obtained in several patients who failed to show any appreciable drop in the eosinophil count. Moderate leucocytosis was observed during therapy in patients suffering from those diffuse "collagen diseases" characterized by leucopenia, and exacerbations were frequently preceded by a decrease in the white count. Albuminuria, hematuria, and cylindruria, when present, always diminished or cleared during treatment, and abnormal plasma proteins showed a tendency to return to normal.

Complications noted during therapy with ACTH and cortisone included salt and water retention, the potassium deficiency syndrome, Cushing's syndrome, and certain psychologic disturbances. While salt and water retention is frequently benefited by mercurials, such diuresis may occur without an increased urinary sodium output and with a moderate increase in urinary excretions of potassium. This makes it important to determine sodium and potassium outputs before, during, and after mercurial diuresis. The syndrome of potassium deficiency may simulate and must be differentiated from the acute surgical abdomen. It is best prevented by the oral administration of potassium chloride or bicarbonate. Once the syndrome develops, it presents a difficult therapeutic problem, requiring the intravenous and oral administration of potassium. The authors believe that the results of this study indicate that ACTH can be safely administered for 2 weeks or less without extensive laboratory control, but that long-term therapy must be carried out only when adequate laboratory facilities are available. Long-term cortisone therapy, because of the lower incidence and mildness of complications, is more suitable for general use. F.

**Pulmonary Infiltration With Blood Eosinophilia.** Sheeran, A. D.: Am. J. M. Sc. **10**: 269, 1951.

Pulmonary infiltration of a shifting nature associated with blood eosinophilia reaching a high of 63 per cent persisted for more than 6 months in a 48-year-old woman. The illness was ushered in by a dry cough and chest pain which lasted for only a short time. Malaise and low-grade fever continued. Various antibiotics, antihistaminics, Adrenalin, and a course of neoarsphenamine did not influence the course of the syndrome. Exhaustive laboratory investigations failed to reveal any significant findings. All skin reactions were negative with the exception of those obtained with a strain of *Streptococcus viridans* cultured from the sputum and with *Escherichia coli* and *Staphylococcus aureus* cultures from maxillary sinus washings. Treatment with an autogenous vaccine made from these organisms was instituted and continued at weekly intervals for 2 months. Definite signs of improvement were apparent 6 weeks after the beginning of therapy. The author is unwilling to draw any definite conclusions regarding the relationship between the clinical improvement and the vaccine therapy, but points out that further investigations in similar cases is warranted. The significant diagnostic features of Loeffler's syndrome and tropical eosinophilia are discussed and the differences between typical examples of these conditions and the case presented are pointed out. F.

**Investigations Into the Histamine Content of Umbilical Blood.** Pettay, O.: Acta pædiat. **39**: 283, 1950.

The histamine content of the plasma obtained from 25 umbilical bloods and from 10 normal adult bloods was determined. The average histamine content of umbilical blood plasma was found to be 2 or 3 times that of normal adult plasma. This marked difference was attributed to the absence of oxygen in the fetal circulation.

A study of various fetal tissues revealed that the lungs contained the greatest amounts of histamine. The amniotic fluid contained large amounts of histaminase. The relationship between the high histamine content of the fetal plasma and various types of birth accidents is discussed. H.

**Iododerma Associated With Loeffler's Syndrome.** Usher, B.: Canad. M. A. J. **64**: 67, 1951.

A case of iododerma associated with extensive but transient pulmonary lesions was observed. Two weeks following the illness there was a blood eosinophilia of 8 per cent. No eosinophils were present in the sputum at this time. Neither blood nor sputum studies were made prior to or during the acute illness. A scratch test performed with 2 per cent iodine one month after the illness gave a negative reaction. The author believed that this is the first reported case of Loeffler's syndrome associated with an allergic reaction to iodine. R. W.

**Effects of X-Irradiation on Passively Transferred Antibody.** Hallingsworth, J. W.: Proc. Soc. Exper. Biol. & Med. **75**: 477, 1950.

Rabbits were injected intravenously with high titered rabbit anti-sheep red cell hemolysin or human brucella immune serum. One day prior to the injection, some of the animals from each group were irradiated with 300 r of x-ray. Study of the antibody titers revealed that the rate of destruction of the homologous antibody was much slower than that of the heterologous anti-

body. No apparent difference was noted between the rate of destruction of antibody in irradiated and in control animals. Twenty-five days after the initial human serum injection, antihuman serum titers were determined in irradiated and control animals. The irradiated animals showed low titers as compared to the controls, indicating that the x-ray dosage was sufficient to decrease the formation of antibody to heterologous serum proteins. B. S.

**Failure of ACTH or Cortisone to Suppress Tuberculin Skin Reactions in Tuberculous Guinea Pigs.** Sheldon, W. H., Cummings, M. M., and Evans, L. D.: Proc. Soc. Exper. Biol. & Med. **75**: 616, 1950.

One month following inoculation with virulent tubercle bacilli, guinea pigs were treated with 2 mg. of ACTH or cortisone twice daily for 6 days. A control group of infected animals did not receive hormone therapy. Both treated and untreated animals showed positive reactions to tuberculin before and 4 days after hormone administration. The size of the tuberculin reaction and the degree of erythema and induration appeared to be less in the guinea pigs receiving hormone. Histologic studies of the skin at the site of the tuberculin reactions showed definite differences in the degree of tissue response between the 2 groups. Proliferation of fibroblasts and endothelium was less active in the lesions of the hormone-treated animals than in those of the control animals. The authors suggested that ACTH and cortisone do not interfere primarily with the immune mechanism of the tuberculin skin reaction but do decrease the associated inflammatory process. B. S.

**Studies of Immunologic Reactions of Patients With Hodgkin's Disease (Antibody Reaction to Typhoid Immunization).** Hoffmann, G., and Rottino, A.: Arch. Int. Med. **86**: 872, 1950.

Thirteen patients with proved Hodgkin's disease were given routine typhoid vaccinations and their antibody titers were measured. The response of these subjects to vaccination was approximately the same as that of a control group. The effect of the administration of nitrogen mustard upon antibody production was difficult to evaluate. Patients with advanced disease showed inability to maintain agglutinins for prolonged periods of time. R. W.